Breast cancer may be linked to mother's childhood

Chemical exposure in past generations could affect present ones, scientists say

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OAKLAND — New thinking on the causes of breast cancer suggests the disease's origins may be found not in anything a woman has done, but in what her mother — and possibly her grandmother — did before her.

The findings further suggest that tiny exposure to hormone-like industrial chemicals early in life can have profound effects not just later in adulthood, but in future generations as well.

Taken as a whole, said scientists gathered today for a conference on early environmental exposures and their link to breast cancer, the research simultaneously offers hope and despair: It points the way to potential new cures while highlighting how little we understand of a pollution pervasive in our bodies and environment.

"We are inducing certain genetic sequences that later on make the animal more susceptible to cancer," said Dr. Jose Russo, director of the Fox Chase Cancer Center in Philadelphia, where some of this research is being done.

"This is not a humongous dose where you kill the animal. These are levels found in the environment, but are enough to change the (genetic) expression," he said.

The current thinking on breast cancer is fairly straightforward: The earlier a girl hits puberty, the greater her odds of getting breast cancer later in life. Scientists generally agree that diet, obesity, lack of exercise and other factors play key roles in the increasingly earlier onset of menarche in girls — sometimes at 8 years or younger, particularly in First World economies.

This new information does not change what is commonly accepted about breast cancer. Rather, it suggests that diet, hormone-like chemicals, and genetic susceptibility interact in ways regulators and scientists do not fully grasp.

Much of the science is a result of an ambitious seven-year, $35 million effort to map the environmental causes of breast cancer. The project is in its fourth year.

Two results in particular are startling.

The first is the notion that these hormone-like chemicals — known as endocrine disruptors and found in everything from shampoo and cosmetics to canned tomato sauce and baby toys — muck with our genes.

They do so not by altering the genes themselves, said Thea Tlsty a pathology professor at University of California, San Francisco, but by influencing the tightly choreographed sequences controlling when genes flip on or off.

It's akin to taking a computer that crunches numbers and reprogramming it to only play music. The computer — the gene, in this case — hasn't changed, but its output has. That, Tlsty said, is what endocrine disruptors do: They alter not the genome, but the epigenome — the program.

Take a crucial protein, HOXA9, known to fight breast cancer cells. In almost all women with breast cancer, Tlsty said, there is no HOXA9 activity, or expression.

But almost half those women have the protein, Tlsty found. It just never flipped on. So what would keep it off? Any of a number of common contaminants, Tlsty said. What's more, the effect was translated across generations, she said. Turn the gene controlling HOXA9 off in a mouse, and that mouse's offspring never express it, either.

It's as if the protein disappeared.

Except that, in the United States, if a chemical altered the gene, it would most likely be banned. There is no standard for chemicals altering the epigene, or program.

The other startling finding concerns timing: A dose of any given pollutant considered inconsequential to an adult — the basis for most regulatory standards — may in fact have considerable consequences when given at or before birth or during adolescence.

At the Cox Center in Philadelphia, Russo's team is feeding laboratory mice small amounts of various common chemicals — dioxins, phthalates, bisphenol-A — at various life stages, including before birth, via the mother.

And while Russo's research deals only with rodents, it suggests there may be factors at play influencing puberty and young girls' development that we do not fully grasp.

"If we can study these things that affect the variability impacting the onset of puberty, we could have a better sense of the factors contributing to breast cancer," said Dr. Frank Biro, a professor of pediatrics at the Cincinnati Children's Hospital.

"We're casting a fairly broad net to try and understand these environmental influences," he said.